

healing and development. Angiogenesis is a complex biological process involving many factors and cell types to produce new blood vessels. Many natural factors have been found to have angiogenic activity including platelet-derived growth factor, fibroblast-derived growth factor, epidermal growth factor, vascular endothelial-derived growth factor, *etc.* Arterial and venous endothelial cells and smooth muscle cells have been found to be sensitive to fluid dynamic shear stress and mechanical strain and to release pro-angiogenic factors (*e.g.*, platelet-derived growth factors A and B, and basic fibroblast growth factor) in response to such stimuli (Davies "Mechanisms involved in endothelial responses to hemodynamic forces" *Atherosclerosis* 131:S15-S17, June 1997; Diamond *et al.* "Tissue plasminogen activator messenger RNA levels increase in cultured human endothelial cells exposed to laminar shear stress" *Journal of Cell Physiology* 143:364-371, 1990; Hsieh *et al.* "Shear stress increases endothelial platelet-derived growth factor mRNA levels" *American Journal of Physiology* 260:H642-H646, 1991; Malek *et al.* "Fluid shear stress differentially modulates expression of genes encoding basic fibroblast growth factor and platelet-derived growth factor B chain in vascular endothelium" *Journal of Clinical Investigation* 92:2013-2021, 1993; Mason "The ins and outs of fibroblast growth factors" *Cell* 78(4):547-552, August 1994; Mitumata *et al.* "Fluid shear stress stimulates platelet-derived growth factor expression in endothelial cells" *American Journal of Physiology* 265(1):H3-H8, July 1993; Sumpio "Hemodynamic forces and the biology of the endothelium: signal transduction pathways in endothelial cells subjected to physical forces in vitro" *Journal of Vascular Surgery* 13(5):744-746, May 1991; Ichioka *et al.* "Effects of shear stress on wound-healing angiogenesis in the rabbit ear chamber" *Journal of Surgical Research* 72:29-35, 1997; each of which is incorporated herein by reference). Shear stress is also instrumental in the control of nitric oxide, endothelin-1, transforming growth factor  $\beta_1$ , and a host of others, many of which may also contribute to angiogenesis.--

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Please substituted the following paragraph for the paragraph beginning on page 5, line 5:

--In a preferred embodiment, the angiogenic factors produced by the vascular cells in response to the external compression include, but are not limited to, growth factors (*e.g.*, platelet-derived growth factor, fibroblast-derived growth factor, epidermal growth factor, vascular